REMARKS

Claims 1-3, 7-32, 36, 37, 42-45, and 75 are pending in the above-referenced application. The Examiner has rejected all the pending claims. Claims 1-3, 30, and 42-45 are amended in this Response; and claim 9 has been canceled. No new claims have been added. Applicant respectfully submits that no new matter is presented with these amendments. Applicant reserves the right to prosecute without prejudice in a future application subject matter amended from the claims by the Amendment submitted herewith. Applicant respectfully requests consideration of the amended claims presented herein and respectfully submits that the amended claims are now in condition for allowance.

I. **Rejections under 35 U.S.C. § 101.** The Examiner has rejected claims 30-32 and 36-37 under 35 U.S.C. § 101. The Examiner maintains that claims 30-32 and 36-37 could be construed to include an organism and as such are drawn to non-statutory subject matter under § 101. However, the Supreme Court has held that organisms altered by the hand of man are patentable. *Diamond v. Chakrabarty*, 206 U.S.P.Q. 193, 197 (U.S. Sup. Ct. 1980). Applicant submits that claim 3-32 and 36-37 as read by one of skill in the art do not read upon non-statutory subject matter since the claimed cells have "less than wild type p21 activity" and have therefore been altered by the hand of man. However, in order to further prosecution, Applicant has amended independent claim 30 to include the term "isolated" so that it is clear the claimed cell is separated from what it is normally associated with in nature. Therefore, amended claim 30 and its dependencies do not read upon non-statutory subject matter. Support for this amendment can be found on page 17, lines 9-19, of the specification as originally filed. Applicant submits that this amendment renders the Examiner's rejection under § 101 moot.

II. **Rejections under 35 U.S.C. § 112, first paragraph.** The Examiner has rejected claims 1-3, 7-29, 42-45, and 75 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner argues that the specification does not provide information such that one of ordinary skill in the art could practice the claimed invention without undue experimentation. Based on the eight factors cited in *In re Wands*, the Examiner maintains that (1) the claimed invention is only enabled for stem cells, not progenitor cells; (2) the specification does not enable the treatment of

any disease, specifically therapeutically effective amounts of cells; and (3) the working examples are limited to hematopoietic cells. Applicant addresses each of the Examiner's concern in turn below.

First, the claims are presently amended to recite only stem cells rendering the Examiner's concerns regarding progenitor cells moot.

Regarding the treatment of disease using the inventive cell with less than wild type p21 activity, Applicant submits that certainly for hematopoietic diseases such as hematologic malignancies, these cells in a pharmaceutical composition could be used in a bone marrow transplant. These cells could also be useful in gene therapies involving hematopoietic cells. Hematopoietic stem cells with less than wild type p21 activity have been found to successfully repopulate the bone marrow in irradiated animals (*e.g.*, Example 3 on page 44-51 of the specification, and the experiments described in the Declaration of Scadden submitted June 22, 2005). Claims 42-45 drawn to pharmaceutical compositions have been amended to recite hematopoietic stem cells based on these findings. Applicant respectfully submits that claims 42-45 are enabled and requests that the rejection be removed.

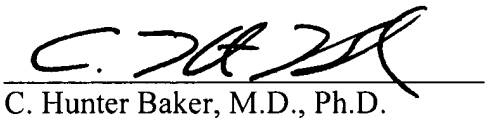
Lastly, although the specification includes only working examples using hematopoietic cells, the literature includes studies examining the role of p21 in other stem cells such as neural stem cells, skin stem cells, and mammary stem cells. *See, e.g.*, Qiu *et al.*, "Regenerative response in ischemic brain restricted by p21cip1/waf1" *J. Exp. Med.* 199(7):937-45, 2004; Kippin *et al.*, "p21 loss compromises the relative quiescence of forebrain stem cell proliferation leading to exhaustion of their proliferation capacity" *Genes Dev.* 19(6):756-67, 2005; Clarke, "Isolation and characterization of human mammary stem cells" *Cell Prolif.* 38:375-86, 2005; Topley *et al.* "$p21^{WAF1/Cip1}$ functions as a suppressor of malignant skin tumor formation and a determinant of keratinocyte stem-cell potential" *Proc. Natl. Acad. Sci. USA* 96:9089-94, August 1999 (a copy of each of these papers has been included herewith). These reports confirm that inhibition of p21 activity in neural, skin, and mammary stem cells leads to an expansion of the stem cell population. In short, in stem cell populations where the experiment of reducing p21 activity has been done, the decrease in p21 promotes proliferation of these cells without a loss of potential. For example, p21 has been shown in neural stem cells to be important in maintaining stem cell quiescence and self-renewal as it has already been demonstrated in hematopoietic stem

cells. Applicant submits that based on these reports which confirm the description in the specification of the role of p21 in other stem cell populations besides hematopoietic cells, the claims are enabled. There is no evidence of record to the contrary. Applicant, therefore, requests that the rejection be removed.

The claims as amended are enabled by the specification as confirmed by either the working examples in the specification or by subsequent reports in peer-reviewed scientific articles. Claims 1-3, 7-29, 42-45, and 75 are now in condition for allowance.

If it is believed that a telephone conversation would expedite matters, the Examiner is invited to contact the undersigned at (617) 248-5215. Although it is believed that there is no fee associated with this amendment, if Applicant is mistaken, please charge any fees to our Deposit Account Number: 03-1721.

Respectfully submitted,



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